



## phosphoribosylpyrophosphate synthetase superactivity

Phosphoribosylpyrophosphate synthetase superactivity (PRS superactivity) is characterized by the overproduction and accumulation of uric acid (a waste product of normal chemical processes) in the blood and urine. The overproduction of uric acid can lead to gout, which is arthritis caused by an accumulation of uric acid crystals in the joints. Individuals with PRS superactivity also develop kidney or bladder stones that may result in episodes of acute kidney failure.

There are two forms of PRS superactivity, a severe form that begins in infancy or early childhood, and a milder form that typically appears in late adolescence or early adulthood. In both forms, a kidney or bladder stone is often the first symptom. Gout and impairment of kidney function may develop if the condition is not adequately controlled with medication and dietary restrictions. People with the severe form may also have neurological problems, including hearing loss caused by changes in the inner ear (sensorineural hearing loss), weak muscle tone (hypotonia), impaired muscle coordination (ataxia), and developmental delay.

### Frequency

PRS superactivity is believed to be a rare disorder. Approximately 30 families with the condition have been reported. More than two thirds of these families are affected by the milder form of the disease.

### Genetic Changes

Certain mutations in the *PRPS1* gene cause PRS superactivity. The *PRPS1* gene provides instructions for making an enzyme called phosphoribosyl pyrophosphate synthetase 1, or PRPP synthetase 1. This enzyme helps produce a molecule called phosphoribosyl pyrophosphate (PRPP). PRPP is involved in producing purine and pyrimidine nucleotides. These nucleotides are building blocks of DNA, its chemical cousin RNA, and molecules such as ATP and GTP that serve as energy sources in the cell. PRPP synthetase 1 and PRPP also play a key role in recycling purines from the breakdown of DNA and RNA, a faster and more efficient way of making purines available.

In people with the more severe form of PRS superactivity, *PRPS1* gene mutations change single protein building blocks (amino acids) in the PRPP synthetase 1 enzyme, resulting in a poorly regulated, overactive enzyme. In the milder form of PRS superactivity, the *PRPS1* gene is overactive for reasons that are not well understood. *PRPS1* gene overactivity increases the production of normal PRPP synthetase 1

enzyme, which increases the availability of PRPP. In both forms of the disorder, excessive amounts of purines are generated.

Under these conditions, uric acid, a waste product of purine breakdown, accumulates in the body. A buildup of uric acid crystals can cause gout, kidney stones, and bladder stones. It is unclear how *PRPS1* gene mutations are related to the neurological problems associated with the severe form of PRS superactivity.

## **Inheritance Pattern**

This condition is inherited in an X-linked pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell sometimes causes the disorder.

In most reported cases, affected individuals have inherited the mutation from a parent who carries an altered copy of the *PRPS1* gene. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons. PRS superactivity may also result from new mutations in the *PRPS1* gene and can occur in people with no history of the disorder in their family.

## **Other Names for This Condition**

- gout, PRPS-related
- PRPP synthetase overactivity
- PRPP synthetase superactivity
- PRPS1 superactivity
- PRS overactivity
- PRS superactivity

## **Diagnosis & Management**

### Genetic Testing

- Genetic Testing Registry: Phosphoribosylpyrophosphate synthetase superactivity <https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970827/>

### Other Diagnosis and Management Resources

- GeneReview: Phosphoribosylpyrophosphate Synthetase Superactivity  
<https://www.ncbi.nlm.nih.gov/books/NBK1973>
- MedlinePlus Encyclopedia: Hearing Loss  
<https://medlineplus.gov/ency/article/003044.htm>
- MedlinePlus Encyclopedia: Movement, Uncoordinated  
<https://medlineplus.gov/ency/article/003198.htm>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

## **Additional Information & Resources**

### MedlinePlus

- Encyclopedia: Hearing Loss  
<https://medlineplus.gov/ency/article/003044.htm>
- Encyclopedia: Movement, Uncoordinated  
<https://medlineplus.gov/ency/article/003198.htm>
- Health Topic: Genetic Brain Disorders  
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Gout  
<https://medlineplus.gov/gout.html>
- Health Topic: Metabolic Disorders  
<https://medlineplus.gov/metabolicdisorders.html>

### Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Gout  
[https://www.niams.nih.gov/Health\\_Info/Gout/](https://www.niams.nih.gov/Health_Info/Gout/)

### Educational Resources

- Disease InfoSearch: Phosphoribosylpyrophosphate synthetase superactivity  
<http://www.diseaseinfosearch.org/Phosphoribosylpyrophosphate+synthetase+superactivity/9104>
- MalaCards: phosphoribosylpyrophosphate synthetase superactivity  
[http://www.malacards.org/card/phosphoribosylpyrophosphate\\_synthetase\\_superactivity](http://www.malacards.org/card/phosphoribosylpyrophosphate_synthetase_superactivity)
- Merck Manual Professional Version: Purine Nucleotide Synthesis Disorders  
<http://www.merckmanuals.com/professional/pediatrics/inherited-disorders-of-metabolism/purine-nucleotide-synthesis-disorders>
- Orphanet: Phosphoribosylpyrophosphate synthetase superactivity  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=3222](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3222)

### Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases  
<http://www.climb.org.uk/>
- Hearing Health Foundation  
<http://hearinghealthfoundation.org/>
- National Ataxia Foundation  
<http://www.ataxia.org/>
- University of Kansas Medical Center: Hearing Loss Resources  
<http://www.kumc.edu/gec/support/hearing.html>

### GeneReviews

- Phosphoribosylpyrophosphate Synthetase Superactivity  
<https://www.ncbi.nlm.nih.gov/books/NBK1973>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28phosphoribosylpyrophosphate+synthetase+superactivity%29+OR+%28prps1+superactivity%29+OR+%28prs+superactivity%29+OR+%28prs+overactivity%29+OR+%28prps-related+go+ut%29+OR+%28prpp+synthetase+superactivity%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

### OMIM

- PHOSPHORIBOSYLPYROPHOSPHATE SYNTHETASE SUPERACTIVITY  
<http://omim.org/entry/300661>

## Sources for This Summary

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